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Wise or wide (WoW) study protocol: a national, multicentre, prospective, randomised and controlled, parallel group, non-inferiority study to compare single-staged versus two-staged excisions of thin invasive (≤1.0 mm) melanoma

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ABSTRACT

Background Sweden has one of the highest incidence rates of cutaneous melanoma globally, and the incidence is rapidly increasing. Melanoma mortality is linked to the thickness of the primary tumour, with thicker melanomas having a poorer prognosis. Thin invasive melanomas (≤1.0 mm Breslow thickness) have excellent prognosis. Traditionally, the surgical approach for melanoma involves a two-step procedure of a diagnostic excision followed by a wide local excision (WLE) with 10 mm clinical margins. The WLE aims to remove potential microsatellites and residual melanoma, which in theory would prevent loco-regional recurrence and could improve survival. However, recent research questions the necessity of WLE for thin invasive melanomas, given their favourable prognosis, minimal risk of microsatellitosis and low rates of residual melanoma found in WLE tissue specimens.

Methods and analysis This multicentre, non-inferiority, randomised controlled trial seeks to enrol 2486 patients with thin invasive melanomas that are completely excised with ≥1.5 mm histopathological margins following the diagnostic excision. Patients will be randomly assigned to either a control group that will undergo a WLE with 10 mm clinical margins according to current clinical routine or an experimental group without a WLE. The primary and secondary endpoints are recurrence-free survival at 5 and 10 years, respectively, with tertiary aims including postoperative complications, scar quality, patient satisfaction and quality of life, healthcare resource utilisation as well as differences in biomarkers of recurrent and non-recurrent melanomas. Patients will be assessed at clinical follow-up visits at 3 months as well as at 1, 2, 3, 5 and 10 years.

Ethics and dissemination Approval of this study was obtained from the Swedish Ethical Review Authority (2024-03274-01). The findings of the study will be presented at international scientific meetings and published in peer-reviewed academic journals.

Trial registration number NCT06363591.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This is a multicentre, parallel group, randomised controlled trial with 10 year follow-up.
⇒ The sample size of 2486 patients provides robust statistical power to establish non-inferiority for omission of wide local excision for the primary and secondary endpoints of recurrence-free survival.
⇒ Participants are randomly assigned in a 1:1 ratio to either the control or experimental group with stratification by study site, Breslow thickness and ulceration, ensuring balanced groups and enhancing the validity of the results.
⇒ As an open-label trial, the awareness of treatment allocation by both participants and investigators introduces potential bias, particularly in subjective tertiary outcomes and participant behaviour, though it is unlikely to significantly impact primary and secondary survival outcomes.

INTRODUCTION

Background and rationale

The overarching aim of this study is to improve the management of cutaneous melanoma (hereinafter 'melanoma') through more effective surgical treatment without compromising prognosis. Sweden has one of the highest incidence rates of melanoma in the world, and the incidence is rapidly increasing.[1] Melanomas with greater extension into the dermis and deeper skin layers are associated with poorer prognosis and lower survival rates as compared with thin tumours.[2] In Sweden, the 10 year melanoma-specific survival rate for patients with thin invasive melanomas (≤1.0 mm

Breslow thickness, hereinafter 'thin melanoma') is >96%–97%.[3 4]

Based on longstanding purely historical reasons, all invasive melanomas, regardless of Breslow thickness, are still excised in a two-staged process according to national and international guidelines. First, a diagnostic excision is performed with 2 mm clinical margins. This is followed by a second wide local excision (WLE) with larger margins of 10–20 mm depending on the thickness of the melanoma. The clinical margins used during WLE have decreased during the past decades, thanks to the findings from large multicentre studies. A meta-analysis based on seven previous randomised controlled trials (RCTs) comparing narrow (10–20 mm) versus wide margins (30–50 mm) showed no significant improvement in recurrence risks, overall survival nor melanoma-specific death with wider margins.[5] As early as 1977, Breslow and Macht suggested using 10 mm clinical margins for thin melanomas based on a smaller case series.[6] Such a recommendation was implemented following a subsequent RCT comparing 30 and 10 mm clinical margins for melanomas with a Breslow thickness<2 mm.[7] Later, trials from the UK and Sweden led to recommendations of 20 mm clinical margins being used for thicker melanomas.[8 9] Currently, an international RCT is investigating the outcomes for patients with T2–T4 melanomas randomised to either 10 or 20 mm clinical margins in the WLE.[10 11]

WLE in melanoma patients, even after a diagnostic excision with clear histopathological margins, strives to remove possible microsatellites and residual melanoma. This approach is based on preventing the theoretical risk of loco-regional recurrence and the potential to improve survival. In thin melanomas, however, microsatellites are only observed in 0.1% of cases according to a recent study including 2359 thin melanomas.[12] In regard to residual melanoma after complete removal in the diagnostic excision, other studies have shown that this only occurred in 0%–0.5% of patients.[13 14] One study found higher rates of residual melanomas in WLE specimens (4.2%), but lentiginous melanomas were the main culprit for this occurring.[15]

In a retrospective study from the Netherlands, after adjusting for age, gender, Breslow thickness and tumour location, no significant differences in overall survival were observed between 182 melanoma patients who did not undergo WLE and 282 controls.[16] Two studies with large cohorts comparing overall survival for melanoma patients treated with WLE or Mohs micrographic surgery with narrow histopathological margins found that this type of surgery did not affect overall survival for patients with melanomas of the head and neck area nor on the trunk and extremities.[17 18] Furthermore, it was recently shown that 25% of patients with thin melanomas undergoing WLE have postoperative morbidities (eg, issues with wound healing, scarring and anxiety) as compared with 0% in a control group with patients who only underwent diagnostic excisions.[19]

It was recently proposed that it is time for a paradigm shift towards 'personalised excision' for melanoma patients, based more on histopathological margins than on clinical margins and taking into account patient morbidity, healthcare costs and actual survival rates.[20] Moreover, the evidence supporting the use of WLEs for melanoma is weak according to a recent review.[21]

To date, no RCTs have examined the omission of WLEs, which could save healthcare resources, minimise complex reconstructions after surgery and reduce postoperative complications without compromising patient safety. Therefore, we plan to carry out a non-inferiority RCT to provide a solid scientific ground for 'wise' one-staged excisions instead of 'wide' two-staged excisions for patients with thin melanomas.

Objectives

The overall aim of this multicentre, randomised, controlled, parallel group, non-inferiority trial is to improve the management of patients with thin melanoma by testing the effectiveness of a simplified surgical treatment.

Primary objective

The primary objective is to compare the 5 year risk of recurrence or death from melanoma following WLE or no WLE in patients with a thin melanoma.

Secondary objective

The secondary objective is to compare the 10 year risk of recurrence or death from melanoma following WLE or no WLE in patients with a thin melanoma.

Tertiary objectives

The tertiary objectives are to investigate: (a) the frequency of postoperative complications 3 months after randomisation; (b) scar length and width as well as scar quality assessed by both patients and clinicians measured with the Patient and Observer Scar Assessment Scale (POSAS), 1 and 3 years after randomisation; (c) patient satisfaction measured with the Functional Assessment of Chronic Illness Therapy-Treatment Satisfaction-Patient Satisfaction (FACIT-TS-PS) 3 months, 1 year and 2 years after randomisation; (d) patient quality of life (QoL) measured with the Functional Assessment of Cancer Therapy-Melanoma (FACT-M) questionnaire 3 months, 1 year and 2 years after randomisation; (e) all-cause mortality at 5 and 10 years; (f) healthcare resource utilisation (direct and indirect costs per patient) in both treatment groups at 5 years and (g) differences in biomarkers of recurrent and non-recurrent melanomas.

Trial design

This national, multicentre, prospective, randomised (1:1) and controlled, parallel group, non-inferiority study will determine if avoiding WLEs in patients with low-risk, thin melanomas is safe, decreases morbidity, increases patient satisfaction and QoL and saves costs.

METHODS: PARTICIPANTS, INTERVENTIONS AND OUTCOMES

Study setting

Participants will be recruited from 15 Swedish dermatology departments (seven university hospitals and eight regional hospitals) between 2024 and 2029 following diagnostic excision and histopathological confirmation of their diagnosis.

Eligibility criteria

Inclusion criteria

Eligible patients need to fulfil all criteria listed below:

1. Diagnosis: recent primary pT1 (Breslow thickness≤1.0 mm) invasive cutaneous melanoma (as determined by a diagnostic excision with subsequent histopathological analysis):
   a. On a body location in which a WLE with a 10 mm clinical margin is feasible and would have been planned according to current standard of care.
   b. Histopathologically verified free margins of at least 1.5 mm.
2. Age: ≥18 years at time of consent.
3. Informed consent: ability to provide informed consent and comply with the treatment protocol and follow-up plan.
4. Life expectancy: ≥5 years from the time of diagnosis.

Exclusion criteria

If any of the listed criteria below are present, the patient is ineligible for study participation.

1. The study lesion:
   a. was partially biopsied prior to the diagnostic excision.
   b. was diagnostically excised with a clinical margin ≥6 mm.
   c. was an invasive melanoma of desmoplastic or lentiginous (ie, lentigo maligna or acral lentiginous) subtype.
   d. was located on digits in which amputation is necessary.
2. The patient
   a. had a previous or concurrent melanoma in situ or invasive melanoma (cutaneous or non-cutaneous).
   b. had physical, clinical, radiographic or pathologic evidence of microsatellite, satellite, in-transit, regional or distant metastatic melanoma.
   c. had a previous or intercurrent solid tumour or haematologic malignancy during the past 5 years except cutaneous squamous cell carcinoma or basal cell carcinoma.
   d. is to receive adjuvant radiotherapy to the primary melanoma site after WLE.

Eligibility criteria for study centres and individuals who will perform the interventions:

Study centres and physicians (ie, dermatologists or surgeons) involved in the trial should have extensive experience in the surgical management and follow-up of patients with primary melanomas.

Interventions

Patients with thin melanomas excised with a histopathologically confirmed margin ≥1.5 mm will be offered the opportunity to participate following informed consent and randomisation (1:1) to either (figure 1):

a. Standard treatment with a WLE of the diagnostic excision scar with a lateral clinical surgical margin of 10 mm and a deep clinical surgical margin down to the muscular fascia as recommended by the Swedish national guidelines.
b. Experimental treatment with no WLE.

The allocated interventions for trial participants in both groups will not be discontinued or modified unless the patient asks to terminate their participation in the trial. In the case of local recurrence or distant metastasis occurring in any trial participant, appropriate surgical and/or oncological treatment should be offered.

Outcomes

Primary outcome

Our primary outcome measure is the recurrence rate observed at 5 years after randomisation, including a comparison between the treatment groups. Recurrence is defined as any presence of local/regional/distant disease or melanoma-specific death.

Secondary outcome

Our secondary outcome measure is the recurrence (as defined above) rate observed at 10 years after randomisation, including a comparison between the treatment groups.

Tertiary outcomes

Our tertiary outcome measures are comparisons between the treatment groups regarding:

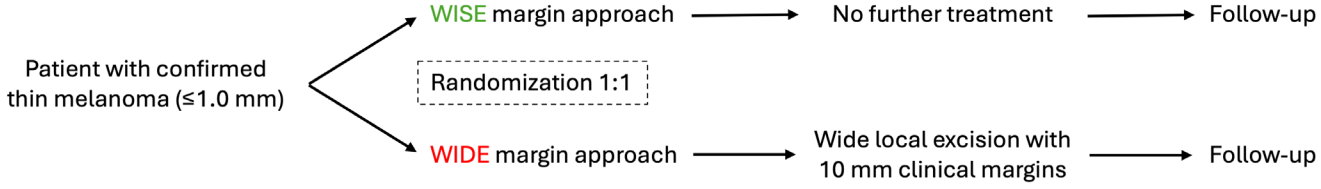

Figure 1 Summary of the randomisation process.

- Frequency and types of postoperative complications 3 months after randomisation.
- Scar length and width (measured in mm) 1 year and 3 years after randomisation.
- Scar quality assessed by both patient and clinician measured with POSAS (online supplemental material 1), which includes several parameters rated by the treating physician and patient on a scale from 1 (normal skin) to 10 (worst scar imaginable) 1 year and 3 years after randomisation.
- Patient satisfaction as measured by the FACIT-TS-PS questionnaire (online supplemental material 2), which includes several parameters with response categories on a 3-point to 5-point scale at 3 months, 1 year and 2 years after randomisation.
- Patients' QoL as measured by the FACT-M questionnaire (online supplemental material 3), which includes several parameters with response categories on a 5-point scale at 3 months, 1 year and 2 years after randomisation.
- Incidence of all-cause mortality 5 and 10 years after randomisation.
- Healthcare resource utilisation in both treatment groups in terms of direct and indirect costs 5 years after randomisation.
- Biomarkers (from biobanks at the respective investigation sites) of comparable melanomas (eg, type, anatomical site and stage) with and without recurrent disease.

Participant timeline

Eligible patients who meet inclusion criteria are provided with information about the trial and guided through informed consent by their treating dermatologist or surgeon during a clinical consultation when they receive their melanoma diagnosis. Participants are to give written consent prior to inclusion.

Follow-up visit assessments

The following frequency for follow-up visits is planned, measured from the time of randomisation. At 3 months, a research nurse or the treating physician conducts a telephone inquiry to assess any early surgical complications (eg, wound infection requiring antibiotic treatment, wound dehiscence/suture rupture, haemorrhage or haematoma, necrosis or delayed secondary intention healing due to hypergranulation). In addition, patients will complete the FACT-M and FACIT-TS-PS questionnaires which can be given to the participant at inclusion, posted via mail or answered electronically.

Clinical follow-up visits will then be scheduled after 1, 2, 3, 5 and 10 years. During each follow-up visit, the physician shall collect an appropriate medical history to rule out symptoms indicating metastatic disease and then perform a total body skin examination including visual and palpatory scar examination and palpation of clinically relevant major lymph node groups. If a local recurrence or any type of metastasis is suspected, biopsies and/or directed radiological examinations should be performed to rule out or confirm recurrence or metastatic spread of the disease. If the patient cannot be followed up at the study site at which they were included, it may be necessary to request any pertinent medical records from the appropriate healthcare provider. At the 1 and 2 year follow-up visits, the FACT-M and FACIT-TS-PS questionnaires shall also be administered and completed. The POSAS questionnaire shall be completed at the 1 and 3 year follow-up visits.

Sample size

For a non-inferiority design assuming recurrence rates of 2.6% in both groups after 5 years (based on follow-up data from a Danish, nationwide, population-based cohort study including 25 720 patients diagnosed with stage IA–IV cutaneous melanoma from 2008 to 2019[22]), a significance level of 0.025, 80% power and a non-inferiority margin of 2%, 1988 patients are required to be included in total (994 in each treatment group) to assess if the recurrence rate in the intervention group is not significantly worse than the control group. The non-inferiority test was based on the Pearson χ^2 test and normal approximation of 95% CI for proportions was applied. PROC POWER in SAS software V.9.4 (SAS Institute, Cary, NC, USA) was used for this calculation. We conservatively estimate that we will have a 20% dropout rate, meaning that an additional 249 patients should be included in each treatment group. Thus, a total of 1243 patients in each treatment group will be included (ie, 2486 patients in total). Calculations were performed in collaboration with statistician Aldina Pivodic at APNC Sweden AB (Mölndal, Sweden).

Recruitment

With >3500 thin invasive melanomas fulfilling the inclusion criteria diagnosed in Sweden each year and 15 major centres (including seven university hospitals) that have accepted to participate, the inclusion period is estimated to span for 4–5 years.

METHODS: ASSIGNMENT OF INTERVENTIONS

Allocation

Participants will be randomly assigned to either the control or experimental groups with a 1:1 allocation in strictly sequential order, stratified by study site, Breslow thickness (>0–0.44, 0.45–0.74 and 0.75–1.0 mm) and ulceration. The random sequence will be computer-generated. The process of allocation will be controlled by an external administrative unit. Allocation concealment will be ensured as treatment assignment will not be revealed in the electronic case report form (eCRF), neither to the enrolment personnel nor the participant, until after the participant has been enrolled and all baseline assessments have been completed.

Blinding

This is an open-label trial.

METHODS: DATA COLLECTION, MANAGEMENT AND ANALYSIS

Data collection methods

The trial will use electronic data capture for data collection. Study sites will be responsible for filling out all relevant fields as outlined in the eCRFs. Periodically, the investigator will be requested to confirm the accuracy of completed eCRFs by signing the indicated forms.

The following data will be collected in the eCRF: (a) background data such as the research participant's age and gender, previous skin cancer, diseases and medication that may affect the risk of complications or recurrence and skin phototype; (b) information about the melanoma, such as size, anatomical location and all histopathological data (eg, subtype, Breslow thickness, possible presence of ulceration, mitoses, regression, etc); (c) close-up and dermoscopic images of the melanoma and images of the surgical scar (excluding images that can identify the research participant) and (d) data from follow-up visits including any postoperative complications, scar width and length, data from POSAS, FACT-M and FACIT-TS-PS, as well as data on any recurrences or deaths. In addition, tissue samples from the tumours, as well as digitised histopathological images ('whole slide images') may be collected in the future for more analyses (eg, further histopathological assessment, biomarker testing, immunohistochemical staining, genetic, molecular, immunological tests and the development of artificial intelligence).

Data management

Participant identification will be replaced by a unique identifier (UID) in order to conceal patient identity. Only authorised personnel will have access to the UID. The participant demographics along with pathology reports with relevant histopathology data will be obtained from medical records and transcribed directly to the eCRF.

As part of the electronic data capture system, electronic administration of QoL and health system resource use questionnaires may be introduced. If a participant enters data into the eCRF for QoL and health system resource use, this will be regarded as source data.

The trial steering committee reserves the right to request copies of select source documents to support the information recorded on the eCRF, as a quality assurance measure. All study-related documentation will be retained by the study site for a duration of 10 years following the completion of the study.

Statistical methods

Data will be analysed in accordance with a prespecified statistical analysis plan (SAP) produced by APNC Sweden AB. Additionally, a separate SAP for cost-effectiveness outcomes will be developed and finalised prior to data analysis. This SAP will be produced by a health economics expert.

Descriptive, continuous variables will be described by mean, SD, median and range, and categorical variables by counts and percentages. All comparisons between treatment groups will be described by relevant effect estimates and 95% CI.

Due to the non-inferiority design, the main analysis will be performed on the per protocol (PP) population for the outcomes where non-inferiority is to be tested. The PP population will include all correctly included and randomised patients in the study who do not have any major protocol violations. These analyses will be performed on an as-treated basis. The final population will be defined at the clean-file meeting in a blinded manner prior to the database lock. Additionally, for robustness and for all outcomes with superiority tests, the analyses will be performed on the intention-to-treat population, including all randomised patients. This analysis will be performed on an as-randomised basis. The safety analyses will be performed on the safety population.

Due to the large sample size, the primary analysis will be tested by using χ^2 tests and the 95% CI will be created by applying normal approximation for the difference in proportions. The study will be considered positive if the upper confidence limit for the difference between the treatment groups does not exceed the predefined non-inferiority margin (ie, 2%).

The following sensitivity analyses will be produced:

1. Risk difference in proportions between the treatment groups applying a generalised linear model with binomial distribution and identity link function adjusted for the randomisation strata. The same non-inferiority margin will be applied.
2. Time to event, adjusting for randomisation strata, applying a Cox proportional hazards model. The proportional hazards assumption will be checked through the addition of an interaction term in the model between the treatment and the log(time). No specific non-inferiority margin is defined for this analysis. The results will be evaluated based on clinical relevance. For descriptive purposes, Kaplan-Meier graphs will be produced.
3. The study site differences and interaction between treatment group and study site will be investigated.

For tests between the two treatment groups with respect to the descriptive baseline variables, χ^2 tests will be used for categorical variables, two-sample t-tests for the normally distributed continuous variables and Mann-Whitney U-tests for the skewed continuous data.

For continuous outcomes, general linear models will be applied, adjusting for randomisation strata. If applicable, the models will be adjusted for the baseline value of the outcome variable. The model applicability will be made by reviewing diagnostic plots. If not fulfilled, non-parametric methods will be applied.

All analyses will be performed by using SAS software V.9.4 or later (SAS Institute, Cary, NC, USA). All tests will be two-tailed and conducted at 0.05 significance level, or one-sided 0.025 level for non-inferiority tests.

Statistical considerations

This study will track the accrual rates to evaluate the feasibility of completing the study. We will regularly report both overall accrual rates and institution-specific rates, with reporting occurring at least annually to the trial steering committee.

To account for potential drop-out rates, we have estimated them to be approximately 20% throughout the trial duration. If necessary, data on patients lost to follow-up will be actively sought through various Swedish databases including Statistics Sweden, SweMR (the nationwide Swedish population-based quality register for cutaneous melanoma) and the Cause of Death Register.

If accrual rates fall short of expectations, we will consider the possibility of terminating the trial prematurely. The decision to do so will be made collaboratively by the principal investigator, John Paoli, in consultation with the trial steering committee. If such a decision is reached, all investigators and participating study sites will be promptly and comprehensively informed, with a thorough explanation provided.

Data monitoring

An independent Data Monitoring Committee (DMC) will oversee the trial's progress, focusing on safety and data review. Member details will be provided before participant enrolment. The DMC's roles include monitoring trial progress, protocol adherence, data quality, site performance and safety, as well as offering recommendations on continuing, modifying or stopping the trial.

Interim analyses

Interim analyses by the DMC will occur every 12 months to assess serious biological and clinical events. Reports will be sent to the trial steering committee, focusing on safety outcomes. These include adverse outcomes, recurrence rates, surgical mortality or morbidity, low patient accrual and the availability of more effective treatments.

Harms

An adverse event (AE) refers to any unfavourable medical occurrence during treatment, not necessarily caused by the treatment. AEs are classified by severity (mild, moderate and severe) and causality (unrelated, possibly related and related). Serious AEs (SAEs) involve life-threatening situations, death or significant disability. All AEs are recorded for 3 months postrandomisation. SAEs must be reported within 24 hours to the sponsor, followed by a detailed report within 7 days.

Auditing

Trial processes and documents will be reviewed annually by the DSMB who will have access to documents in the eCRF in order to promote data quality.

Ethics and dissemination

Research ethics approval

Ethics approval has been obtained from the Swedish Ethical Review Authority (2024-03274-01) and the trial will adhere to the Declaration of Helsinki—ethical principles for medical research involving human subjects.

Protocol amendments

The trial steering committee has exclusive authority to make changes and amendments to the protocol. Prior to implementation, any amendments must receive approval from the Swedish Ethical Review Authority. In cases where an amendment necessitates modifications to the participant information sheet and/or consent form, the investigator must obtain approval or guidance on the revised consent form before making the change. Furthermore, any necessary adjustments to the eCRF will be included as part of the amendment process.

Consent

All study site investigators involved in the trial have the responsibility to ensure that the patient's written informed consent is acquired prior to their involvement in the study.

Confidentiality

The trial will be carried out in accordance with relevant Privacy Acts and Regulations. Data produced during the trial will be kept confidential and all information gathered will be securely stored at the participating centres and in the eCRF system REDCap (REDCap, Research Electronic Data Capture; projectredcap.org), with access restricted to personnel directly engaged in the study.

Declaration of interests

The investigators have no conflicts of interest to declare.

Access to data

Data access will only be available to authorised reviewers.

Ancillary and post-trial care

This is not relevant since all patients are insured through the national health system.

Dissemination policy

Findings will be disseminated through presentations at medical conferences and publication in peer-reviewed scientific journals.

Patient and public involvement

Representatives from the Swedish Melanoma Association (Melanomföreningen) have expressed their support for the study, emphasising its significance for both patients and society. They are keen to follow its progress and engage with future findings to inform the wider patient community. Their contribution may include offering insights into recruitment strategies, providing feedback on the clarity of data collection tools and assisting in the interpretation of findings where feasible. This collaboration seeks to ensure that the results are both meaningful and can be translated into practice in a way that benefits the patient community.

We used the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) checklist when writing our report.[19]

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Contributors JP conceptualised the study, provided overall supervision and is the guarantor of the work. All authors contributed to the study design and methodology. All authors drafted, critically reviewed and approved the final manuscript. ChatGPT 4.0 was used to help translate the patient consent form from Swedish to English.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting or dissemination plans of this research. Refer to the Methods section for further details.

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REFERENCES

1 Cancer statistics database. The Swedish Cancer Registry of the National Board of Health and Welfare, 2022. Available: http://www.socialstyrelsen.se
2 Gershenwald JE, Scolyer RA, Hess KR, *et al*. Melanoma staging: Evidence-based changes in the American Joint Committee on Cancer eighth edition cancer staging manual. *CA Cancer J Clin* 2017;67:472–92.
3 Claeson M, Gillstedt M, Whiteman DC, *et al*. Lethal Melanomas: A Population-based Registry Study in Western Sweden from 1990 to 2014. *Acta Derm Venereol* 2017;97:1206–11.
4 Isaksson K, Mikiver R, Eriksson H, *et al*. Survival in 31 670 patients with thin melanomas: a Swedish population-based study. *Br J Dermatol* 2021;184:60–7.
5 Hanna S, Lo SN, Saw RP. Surgical excision margins in primary cutaneous melanoma: A systematic review and meta-analysis. *Eur J Surg Oncol* 2021;47:1558–74.
6 Breslow A, Macht SD. Optimal size of resection margin for thin cutaneous melanoma. *Surg Gynecol Obstet* 1977;145:691–2.
7 Veronesi U, Cascinelli N, Adamus J, *et al*. Thin stage I primary cutaneous malignant melanoma. Comparison of excision with margins of 1 or 3 cm. *N Engl J Med* 1988;318:1159–62.
8 Gillgren P, Drzewiecki KT, Niin M, *et al*. 2-cm versus 4-cm surgical excision margins for primary cutaneous melanoma thicker than 2 mm: a randomised, multicentre trial. *Lancet* 2011;378:1635–42.
9 Hayes AJ, Maynard L, Coombes G, *et al*. Wide versus narrow excision margins for high-risk, primary cutaneous melanomas: long-term follow-up of survival in a randomised trial. *Lancet Oncol* 2016;17:184–92.
10 Melmar T. Melanoma Margins Trial Investigating 1cm v 2cm Wide Excision Margins for Primary Cutaneous Melanoma (MelMarT), 2021. Available: https://clinicaltrials.gov/ct2/show/NCT02385214
11 Moncrieff MD, Gyorki D, Saw R, *et al*. 1 Versus 2-cm Excision Margins for pT2-pT4 Primary Cutaneous Melanoma (MelMarT): A Feasibility Study. *Ann Surg Oncol* 2018;25:2541–9.
12 Riquelme-Mc Loughlin C, Sandoval-Clavijo A, Blanco de Tord M, *et al*. Prognostic role of microsatellites in melanoma and implications in the American Joint Committee on Cancer classification system: A cohort study. *J Am Acad Dermatol* 2023;88:338–47.
13 de Waal AC, Vossen R, Aben KKH, *et al*. Limited role for histopathological examination of re-excision specimens of completely excised melanomas. *Virchows Arch* 2014;465:225–31.
14 McGoldrick RB, Ng D, Sawyer A, *et al*. Malignant melanoma re-excision specimens: is there a need for histopathological analysis? *J Plast Reconstr Aesthet Surg* 2008;61:983–4.
15 Bolshinsky V, Lin MJ, Serpell J, *et al*. Frequency of residual melanoma in wide local excision (WLE) specimens after complete excisional biopsy. *J Am Acad Dermatol* 2016;74:102–7.
16 Haniff J, de Vries E, Claassen ATPM, *et al*. Non-compliance with the re-excision guidelines for cutaneous melanoma in The Netherlands does not influence survival. *Eur J Surg Oncol* 2006;32:85–9.
17 Demer AM, Hanson JL, Maher IA, *et al*. Association of Mohs Micrographic Surgery vs Wide Local Excision With Overall Survival Outcomes for Patients With Melanoma of the Trunk and Extremities. *JAMA Dermatol* 2021;157:84–9.
18 Hanson J, Demer A, Liszewski W, *et al*. Improved overall survival of melanoma of the head and neck treated with Mohs micrographic surgery versus wide local excision. *J Am Acad Dermatol* 2020;82:149–55.
19 Lau KL, Bradish T, Rannan-Eliya S. “Primum non nocere”: how harmless is routine wide local excision for AJCC stage IA melanoma? *Ann R Coll Surg Engl* 2020;102:483–7.
20 Weyers W. “Personalized Excision” of Malignant Melanoma-Need for a Paradigm Shift in the Beginning Era of Personalized Medicine. *Am J Dermatopathol* 2019;41:884–96.
21 Zijlker LP, Eggermont AMM, van Akkooi ACJ. The end of wide local excision (WLE) margins for melanoma? *Eur J Cancer* 2023;178:82–7.
22 Helvind NM, Brinch-Møller Weitemeyer M, Chakera AH, *et al*. Stage-Specific Risk of Recurrence and Death From Melanoma in Denmark, 2008-2021: A National Observational Cohort Study of 25 720 Patients With Stage IA to IV Melanoma. *JAMA Dermatol* 2023;159:1213–22.